A 54-year-old woman comes to the clinic due to difficulty hearing for the past few weeks. During the neurologic examination, the physician assesses her hearing using a vibrating tuning fork. The handle of the tuning fork is placed on her left mastoid process until the sound is no longer audible. The tines are then quickly placed near the patient's left auditory meatus, and she reports hearing no sound. When the handle of the vibrating fork is placed on the middle of her forehead, she hears the vibration more strongly in her left ear than her right. This patient is most likely experiencing which of the following types of hearing loss?

A. Conductive loss in both ears
B. Conductive loss in left ear
C. Conductive loss in right ear
D. Sensorineural loss in both ears
E. Sensorineural loss in left ear
F. Sensorineural loss in right ear

Submit

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- A. Conductive loss in both ears (0%)
- ✓ B. Conductive loss in left ear (68%)
- C. Conductive loss in right ear (5%)
- D. Sensorineural loss in both ears (1%)
- E. Sensorineural loss in left ear (20%)
- F. Sensorineural loss in right ear (3%)

Omitted
Correct answer
B

68%
Answered correctly

04 secs
Time Spent

05/03/2020
Last Updated

Explanation

Interpretation of Weber & Rinne tests		
	Rinne result	Weber result

Interpretation of Weber & Rinne tests		
	Rinne result	**Weber result**
Normal	AC >BC bilaterally	Midline
Sensorineural hearing loss		Lateralizes to **unaffected** ear
Conductive hearing loss	BC >AC in **affected** ear, AC >BC in unaffected ear	Lateralizes to **affected** ear

AC = air conduction; BC = bone conduction.

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Hearing loss is classified as either conductive (impaired transmission of air vibrations to inner ear) or sensorineural (involving the cochlea or auditory nerve). The Rinne and Weber tests can be used to help determine the type of hearing loss.

The **Rinne test** compares air versus bone conduction (via the mastoid bone). As the vibration of the tuning fork fades, air-conducted sound is normally louder and heard longer than bone-conducted sound. The Rinne test is considered positive (normal) if the sound is heard best at the external auditory meatus (air conduction) and negative (abnormal) if the patient hears the vibration better at the mastoid (bone conduction).

- Bone conduction greater than air conduction suggests conductive hearing loss.

The **Weber test** is performed by placing a vibrating tuning fork on the middle of forehead equidistant from both ears. The vibration carried by bone conduction is normally heard equally in both ears; vibration heard louder in one ear is abnormal.

- Conductive hearing loss causes lateralization to the affected ear as the conduction deficit masks the ambient noise in the room, allowing the vibration to be better heard.

AC = air conduction; BC = bone conduction.

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Hearing loss is classified as either conductive (impaired transmission of air vibrations to inner ear) or sensorineural (involving the cochlea or auditory nerve). The Rinne and Weber tests can be used to help determine the type of hearing loss.

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The **Weber test** is performed by placing a vibrating tuning fork on the middle of forehead equidistant from both ears. The vibration carried by bone conduction is normally heard equally in both ears; vibration heard louder in one ear is abnormal.

- Conductive hearing loss causes lateralization to the affected ear as the conduction deficit masks the ambient noise in the room, allowing the vibration to be better heard.
- Sensorineural hearing loss causes lateralization to the unaffected ear as the unimpaired inner ear can better sense the vibration.

The Rinne test is abnormal in this patient's left ear, and the Weber test lateralizes to her left ear. These findings suggest **conductive hearing loss** in the left ear.

Educational objective:
In conductive hearing loss, bone conduction will be greater than air conduction (abnormal Rinne test), and the Weber test will lateralize to the affected ear. In sensorineural hearing loss, air conduction will be greater than bone conduction (normal Rinne test), and the Weber test will lateralize to the unaffected ear.

Physiology	Ear, Nose & Throat (ENT)	Hearing loss
Subject	System	Topic

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In an animal experiment the levels of various endogenous compounds are measured in the spinal fluid after application of noxious stimuli. One of the compounds that increase as a result of the experiment is a pentapeptide with a strong affinity to delta- and mu-receptors. Which of the following substances is most likely to have a common molecular origin with the pentapeptide described above?

A. Prolactin

B. TSH

C. ACTH

D. Growth hormone

E. Vasopressin

F. Somatomedin C

Submit

In an animal experiment the levels of various endogenous compounds are measured in the spinal fluid after application of noxious stimuli. One of the compounds that increase as a result of the experiment is a pentapeptide with a strong affinity to delta- and mu-receptors. Which of the following substances is most likely to have a common molecular origin with the pentapeptide described above?

A. Prolactin (5%)

B. TSH (5%)

✓ C. ACTH (29%)

D. Growth hormone (9%)

E. Vasopressin (13%)

F. Somatomedin C (36%)

Omitted
Correct answer
C

29%
Answered correctly

02 secs
Time Spent

02/03/2020
Last Updated

Explanation

Enkephalins, endorphins, and dynorphins are endogenous opioid peptides that are part of the body's naturally occurring opioid system. These endogenous peptides are released in response to noxious stimuli and bind to different opioid receptors to allow physiologic modulation of pain. Several different types of opioid receptors have been identified and include mu, delta, kappa, and N/OFQ receptors. Available narcotics like morphine and hydromorphone produce therapeutic analgesic effects by binding to mu receptors and modulating pain perception. Endogenous opioid peptides also play a significant role in gastrointestinal, endocrine, autonomic, and emotional function. Beta-endorphin is one endogenous

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(Choice A) Prolactin is a somatotropic hormone synthesized in the anterior pituitary and is responsible for breast development and milk production. It is structurally similar to growth hormone.

(Choice B) TSH is a glycoprotein hormone synthesized in the anterior pituitary and is responsible for stimulating the secretion of thyroid hormone. It is also responsible for growth of the thyroid gland.

(Choice D) Growth hormone belongs to the family of somatotropic hormones. It is synthesized in the anterior pituitary and is responsible for overall body growth.

(Choice E) Vasopressin, also known as antidiuretic hormone (ADH), is a hormone synthesized in the hypothalamus and released from the posterior pituitary. It primarily functions to regulate fluid retention in the kidneys, but also causes arteriolar contraction of smooth muscle resulting in a pressor effect.

(Choice F) Somatomedin C is a peptide that is structurally similar to insulin. Also referred to as insulin like growth factor, somatomedin C is released in response to growth hormone and stimulates growth in target cells.

Educational Objective:
Beta-endorphin is one endogenous opioid peptide that is derived from proopiomelanocortin (POMC). POMC is a polypeptide precursor that goes through enzymatic cleavage and modification to produce not only beta-endorphins, but also ACTH and MSH. The fact that beta-endorphin and ACTH are derived from the same precursor suggests that there may be a close physiological relationship between the stress axis and the opioid system.

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Beta-endorphin is one endogenous opioid peptide that is derived from proopiomelanocortin (POMC). POMC is a polypeptide precursor that goes through enzymatic cleavage and modification to produce not only beta-endorphins, but also ACTH and MSH. The fact that beta-endorphin and ACTH are derived from the same precursor suggests that there may be a close physiological relationship between the stress axis and the opioid system.

Physiology	Nervous System	Opioids
Subject	System	Topic

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A 37-yearold man comes to the office due to difficulty sleeping. He says that his new job as a business executive is very stressful and requires considerable travel. During the past 3 months, the patient has made numerous trips between the United States and France. He experiences insomnia and daytime sleepiness for several days after these trips, but his sleep then improves significantly. Which of the following hypothalamic nuclei is most likely responsible for this delayed improvement in his symptoms?

A. Anterior

B. Lateral

C. Posterior

D. Suprachiasmatic

E. Supraoptic

F. Ventromedial

Submit

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- A. Anterior (1%)
- B. Lateral (1%)
- C. Posterior (3%)
- ✓ D. Suprachiasmatic (83%)
- E. Supraoptic (6%)
- F. Ventromedial (4%)

Omitted
Correct answer
D

83%
Answered correctly

01 sec
Time Spent

04/08/2020
Last Updated

Explanation

Major functions of hypothalamic nuclei	
Ventromedial	Mediates satiety; destruction leads to hyperphagia
Lateral	Mediates hunger; destruction leads to anorexia

Major functions of hypothalamic nuclei	
Ventromedial	Mediates satiety ; destruction leads to hyperphagia
Lateral	Mediates hunger; destruction leads to anorexia
Anterior	Mediates heat dissipation; destruction leads to hyperthermia
Posterior	Mediates heat conservation; destruction leads to hypothermia
Arcuate	Secretion of dopamine (inhibits prolactin), GHRH
Medial preoptic	Secretion of GnRH, regulates sexual behavior
Paraventricular	Secretion of oxytocin, CRH, TRH & small amounts of ADH
Supraoptic	Secretion of ADH & small amounts of oxytocin
Suprachiasmatic	Circadian rhythm regulation & pineal gland function

ADH = antidiuretic hormone; CRH = corticotropin-releasing hormone; GHRH = growth hormone-releasing hormone; GnRH = gonadotropin-releasing hormone; TRH = thyrotropin-releasing hormone.

This patient is experiencing **jet lag**, a syndrome associated with long flights that cross several time zones. Symptoms include **insomnia**, **daytime drowsiness**, decreased work performance, gastrointestinal issues, and generalized malaise. Jet lag is caused by **dyssynchrony** between the body's circadian rhythms (eg, sleep/wake cycle) and the local environment (eg, daylight hours, sleep schedules).

Circadian rhythms are maintained by the **suprachiasmatic nucleus** (SCN). The SCN receives input from the retina and sends projections to other hypothalamic nuclei and the pineal gland. The primary functions of the SCN are to modulate body temperature and produce hormones such as cortisol (stress hormone) and **melatonin** (sleep-inducing hormone). Circulating melatonin levels are normally highest during the night and lowest during the day. In contrast, cortisol peaks in the morning and reaches its lowest level at night.

In patients with jet lag, the suprachiasmatic nucleus eventually **resynchronizes** the body clock to coincide with the environment over the course of several days. Eastward travel takes longer to recover from than westward travel because it is easier to lengthen the natural sleep/wake cycle than

Supraoptic	Secretion of ADH & small amounts of oxytocin
Suprachiasmatic	Circadian rhythm regulation & pineal gland function

ADH = antidiuretic hormone; CRH = corticotropin-releasing hormone; GHRH = growth hormone-releasing hormone; GnRH = gonadotropin-releasing hormone; TRH = thyrotropin-releasing hormone.

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In patients with jet lag, the suprachiasmatic nucleus eventually **resynchronizes** the body clock to coincide with the environment over the course of several days. Eastward travel takes longer to recover from than westward travel because it is easier to lengthen the natural sleep/wake cycle than to shorten it. Treatment with **melatonin** supplementation can improve the symptoms of insomnia associated with jet lag.

Educational objective:
The suprachiasmatic nucleus regulates circadian rhythms by processing light information from the retina and modulating body temperature and the production of hormones (eg, cortisol, melatonin). Dyssynchrony between the local environment (eg, daylight hours, sleep schedules) and internal circadian rhythms can cause insomnia and daytime sleepiness (ie, jet lag). Melatonin supplementation is recommended for the treatment of insomnia associated with jet lag.

Physiology	Nervous System	Circadian rhythm
Subject	System	Topic

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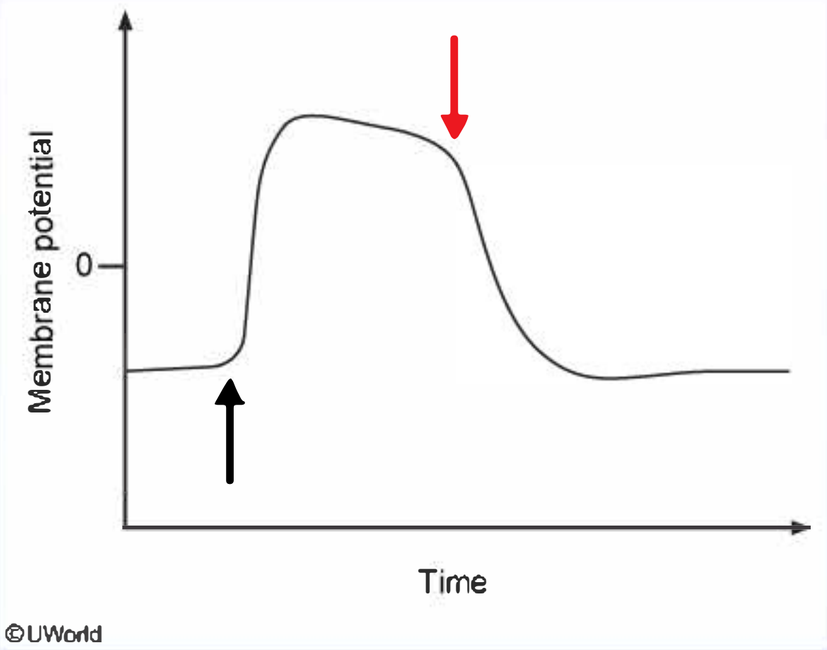
Researchers are studying how the membrane potential of a postsynaptic neuron changes in response to neurotransmitter stimulation. Baseline measurements determine that the resting membrane potential is generated by high membrane permeability for a particular ion. When neurotransmitter stimulation begins, ligand-gated ion channels open (black arrow) and increase the membrane permeability for a different ion, causing a change in membrane potential. This triggers the delayed opening of voltage-gated ion channels (red arrow), which increase the membrane permeability for a third type of ion. The results of the experiment are shown in the graph below.



The equilibrium potentials of different ions under physiologic conditions are as follows:

E_{Na} = +60 mV

E_{K} = −90 mV

E_{Cl} = −75 mV

The equilibrium potentials of different ions under physiologic conditions are as follows:

E_{Na} = +60 mV

E_K = −90 mV

E_{Cl} = −75 mV

E_{Ca} = +125 mV

Which of the following options would best explain the changes in this neuron's membrane potential during the experiment?

	Resting membrane permeability	Ligand-gated ion channel permeability	Voltage-gated ion channel permeability
A.	Sodium	Calcium	Chloride
B.	Sodium	Calcium	Potassium
C.	Potassium	Calcium	Sodium
D.	Potassium	Sodium	Calcium
E.	Potassium	Sodium	Chloride

Submit

The equilibrium potentials of different ions under physiologic conditions are as follows:

E_{Na} = +60 mV

E_{K} = −90 mV

E_{Cl} = −75 mV

E_{Ca} = +125 mV

Which of the following options would best explain the changes in this neuron's membrane potential during the experiment?

	Resting membrane permeability	Ligand-gated ion channel permeability	Voltage-gated ion channel permeability
A. (2%)	Sodium	Calcium	Chloride
B. (17%)	Sodium	Calcium	Potassium
C. (15%)	Potassium	Calcium	Sodium
D. (31%)	Potassium	Sodium	Calcium
✓ E. (32%)	Potassium	Sodium	Chloride

Omitted
Correct answer
E

32%
Answered correctly

06 secs
Time Spent

02/25/2020
Last Updated

Explanation

Equilibrium potentials of cellular ions reflect how they affect the membrane potential if the membrane were permeable solely for that ion. The resting membrane potential shown in the graph is negative, indicating that at rest, the membrane is permeable to an ion with a **negative equilibrium potential** (potassium or chloride). Opening of ligand-gated ion channels in response to neurotransmitter binding (black arrow) causes an increase in membrane potential to above zero. This indicates that the membrane has become permeable for an ion with a **positive equilibrium potential** (sodium or calcium). Opening of voltage-gated ion channels in response to the change in membrane potential (red arrow) causes a drop in membrane potential, indicating that the membrane becomes permeable to an ion with a **negative equilibrium potential** (potassium or chloride).

(Choices A and B) If the membrane were permeable for sodium at rest, the resting membrane potential would be positive as the equilibrium potential of sodium is +60 mV.

(Choices C and D) Had the membrane become more permeable for calcium or sodium following the opening of the voltage-gated ion channels, the membrane potential would have remained positive as both ions have positive equilibrium potentials.

Educational objective:
Changes in membrane potential occur in response to changes in neuronal membrane permeability to various cellular ions. The more permeable the membrane becomes for a cellular ion, the more that ion's equilibrium potential contributes to the total membrane potential.

Physiology	Nervous System	Resting membrane potential and action potential
Subject	System	Topic

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A 45-year-old man comes to the office for followup. He was diagnosed with focal epilepsy 2 years ago and has been treated with several antiepileptic medications. Over the last 6 months, his seizure frequency has increased despite compliance with medical therapy. Neurologic examination and brain imaging are unremarkable. The patient is started on a new antiepileptic medication that selectively blocks voltage-gated calcium channels. This medication most likely affects which of the following steps of neurotransmission?

A. Axonal propagation of the action potential

B. Axonal transport of the neurotransmitter vesicles

C. Fusion and release of neurotransmitter vesicles

D. Neurotransmitter synthesis and packaging into vesicles

E. Release of calcium from the endoplasmic reticulum

Submit

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- A. Axonal propagation of the action potential (7%)
- B. Axonal transport of the neurotransmitter vesicles (4%)
- ✓ C. Fusion and release of neurotransmitter vesicles (76%)
- D. Neurotransmitter synthesis and packaging into vesicles (3%)
- E. Release of calcium from the endoplasmic reticulum (8%)

Omitted
Correct answer
C

76%
Answered correctly

02 secs
Time Spent

03/30/2020
Last Updated

Explanation

Neurons communicate with each other via synapses, regions where the axon terminal of a presynaptic neuron transmits chemical signals to the dendrites of a postsynaptic neuron. Binding of an excitatory neurotransmitter (eg, glutamate) to a postsynaptic neuron causes opening of ligand gated sodium channels, leading to sodium influx and membrane depolarization. This depolarization impulse is transmitted from the dendrites through the cell body to the axon hillock, which contains a large number of voltage-gated sodium channels. Once the axon hillock becomes sufficiently depolarized, an action potential is triggered and propagates along the axon via a steady influx of sodium ions. When the action potential reaches the axon terminal, **voltage-gated calcium channels** open and allow the influx of calcium, which is essential for the fusion and

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Seizures occur due to abnormal, synchronized firing of hyperexcitable neurons in the brain, and many antiepileptic medications work by modifying electrochemical transmission between neurons. Gabapentin is an anticonvulsant that works by inhibiting presynaptic voltage-gated calcium channels, whereas levetiracetam acts downstream by disrupting vesicle fusion.

(Choice A) Antiepileptic medications such as phenytoin and carbamazepine disrupt the generation and propagation of action potentials (in the axon hillock and axon proper, respectively) by blocking voltage-gated sodium channels.

(Choices B and D) Neurotransmitters are synthesized in the presynaptic neuronal cell body and transported to the axon terminal (via kinesin motor proteins), where they are packaged in synaptic vesicles and primed for release.

(Choice E) Although the endoplasmic reticulum contains calcium release channels, these do not directly participate in neurotransmission. Release of calcium from the endoplasmic reticulum is more important for skeletal muscle contraction.

Educational objective:
Voltage-gated sodium channels are important for the generation and propagation of action potentials. When the action potential reaches the axon terminal, voltagegated calcium channels open and allow the influx of calcium, which is essential for the fusion and release of neurotransmitter vesicles into the synaptic cleft.

References

- Targets for antiepileptic drugs in the synapse.
- Research advances in basic mechanisms of seizures and antiepileptic drug action.

A 44-year-old woman comes to the office for follow-up. The patient sustained a complete C7 spinal cord injury a year ago after falling off a cliff while hiking. She is able to move her shoulders and upper arms but has paraplegia and uses a wheelchair. The patient has a suprapubic catheter due to neurogenic bladder. She has no other medical conditions. She is a lifelong nonsmoker. Which of the following changes in respiratory parameters are most likely present in this patient?

	Maximal inspiratory pressure	Maximal expiratory pressure
A.	Decreased	Increased
B.	Decreased	Normal
C.	Normal	Decreased
D.	Increased	Decreased
E.	Increased	Increased

Submit

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	Maximal inspiratory pressure	Maximal expiratory pressure
A. (6%)	Decreased	Increased
B. (36%)	Decreased	Normal
✓ C. (50%)	Normal	Decreased
D. (5%)	Increased	Decreased
E. (1%)	Increased	Increased

Omitted
Correct answer
C

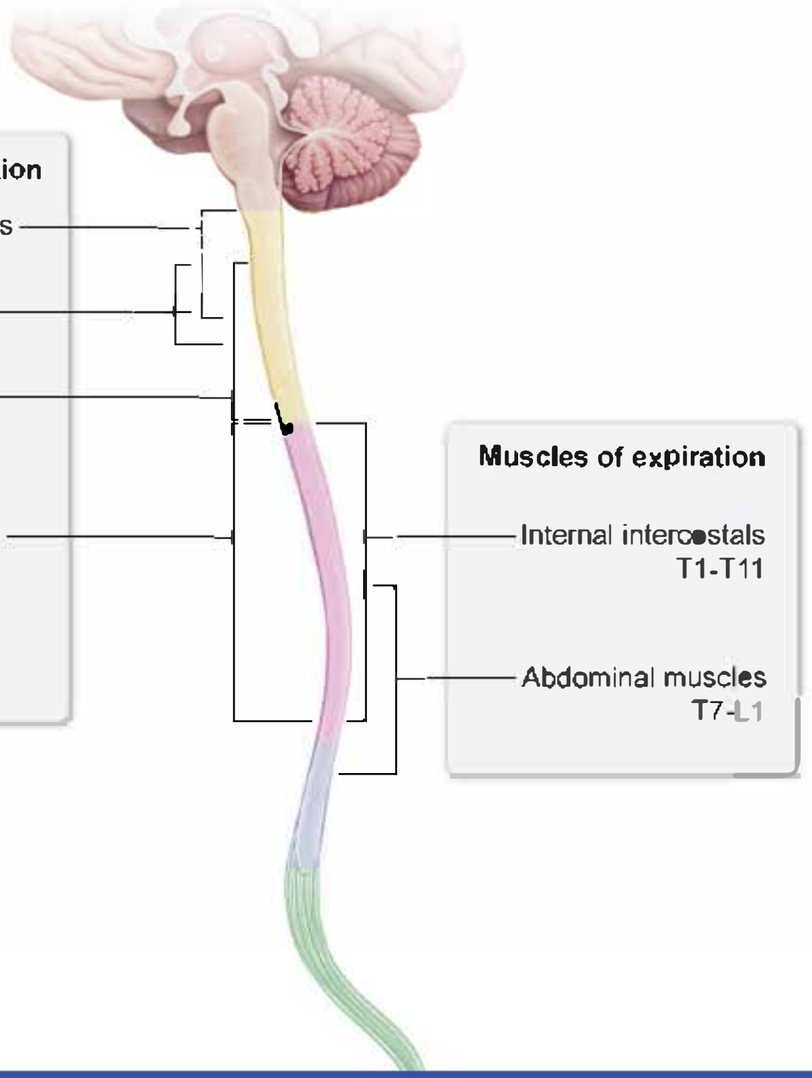
50%
Answered correctly

01 sec
Time Spent

05/28/2020
Last Updated

Explanation

Respiratory muscle innervation



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Patients with **spinal cord injuries** often have significant alterations in **respiratory dynamics**. Because different muscles (with different sources of innervation) control inspiration and expiration, respiratory function is differentially impaired based on the level of spinal cord injury.

Inspiration is driven by an increase in intrathoracic volume. This is mediated predominantly by contraction of the **diaphragm**, which is innervated by the **phrenic nerve** that originates from the **C3-C5** nerve rootlets. Accessory muscles of inspiration elevate the sternum and ribs to further expand the thoracic cavity. These include the external intercostals (innervated by thoracic nerve roots), the sternocleidomastoid (innervated by C1-C4), and the scalenes (innervated by C4-C8).

Passive expiration is driven by the net intrinsic elastic recoil of the lungs, chest wall, ribs, and diaphragm and therefore requires no innervation. **Active expiration**, as measured in this patient's pulmonary function testing, recruits the musculature to pull the ribs down and compress the abdominal contents to push the diaphragm up and decrease intrathoracic volume. This is driven by the **internal intercostals** (innervated by **thoracic nerve roots**) and **abdominal muscles** (innervated by **thoracic and lumbar nerve roots**).

Because the spinal cord injury was at the **level of C7** in this patient, the diaphragm and many of the accessory inspiratory muscles are likely functional, resulting in minimal impairment of maximal inspiratory pressure. However, the muscles involved in active expiration (ie, internal intercostals and abdominal muscles) are likely significantly impaired, leading to a significant **decrease in maximal expiratory pressure**.

(Choices A and B) Although the external intercostals are innervated by thoracic nerve roots and may be impaired in this patient, the other accessory muscles of inspiration, including the sternocleidomastoid and scalenes, are typically able to compensate for their loss and adequately elevate the sternum/ribs. This leads to minimal or no change in the maximal inspiratory pressure.

Educational objective:
The diaphragm is the principal muscle of inspiration and is innervated by the phrenic nerve, which originates from the C3-5 nerve rootlets. Although expiration is largely achieved through passive recoil, active expiration is aided by the internal intercostals (innervated by thoracic nerve rootlets) and abdominal muscles (innervated by thoracic and lumbar nerve roots).

Physiology	Nervous System	Spinal cord injury
Subject	System	Topic

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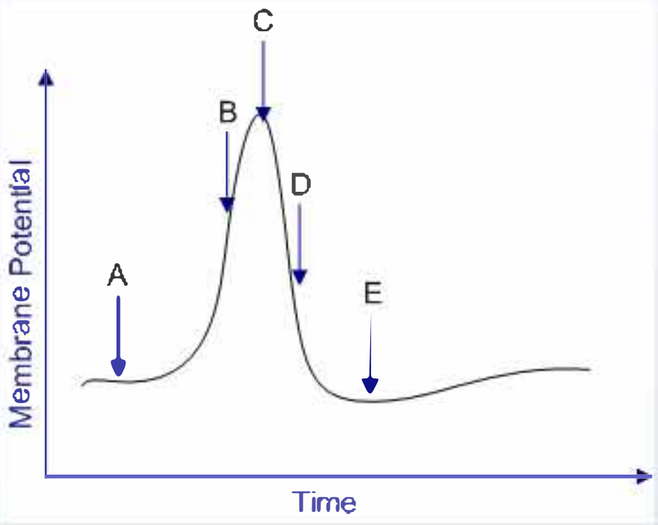
Neurophysiologists are studying recordings of the membrane potential from a giant squid axon. A portion of their recordings is shown on the slide below.



The membrane is most permeable to potassium ions at which of the following points?

A. A
B. B
C. C
D. D
E. E

Submit

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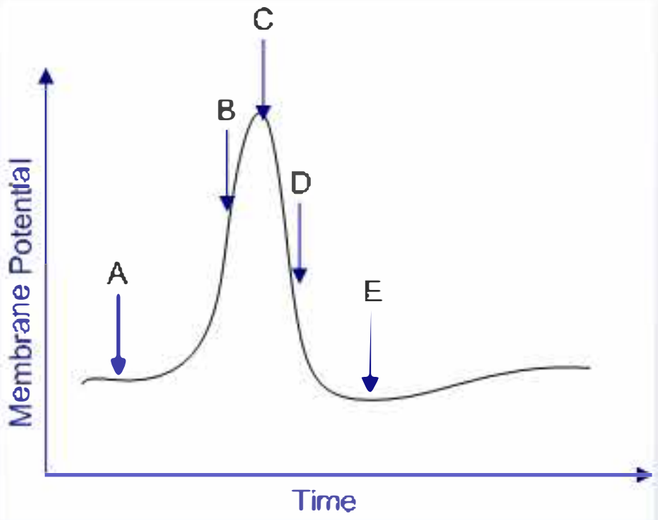


The membrane is most permeable to potassium ions at which of the following points?

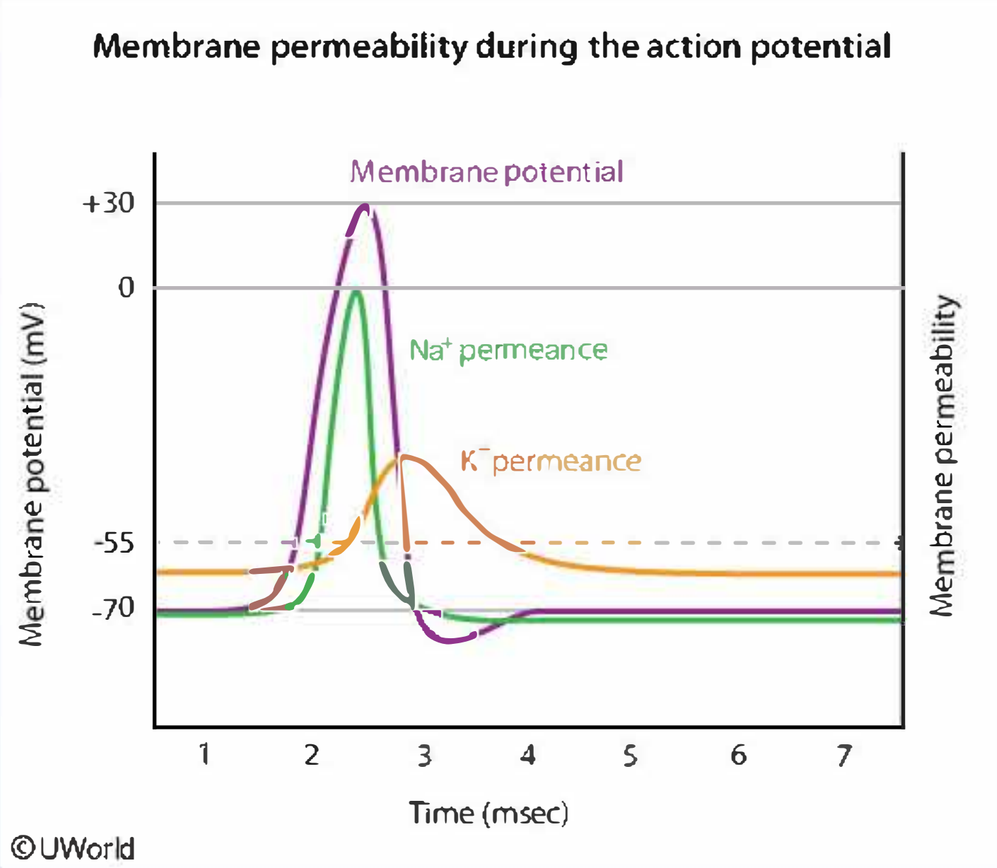
A. A (2%)
B. B (2%)
C. C (17%)
D. D (67%)
E. E (8%)

Omitted
Correct answer

67%
Answered correctly

03 secs
Time Spent

06/28/2020
Last Updated



The graph depicts the potential voltage changes across a cell membrane; these changes (depolarization, repolarization, hyperpolarization, and resting potential) are collectively known as the action potential. The action potential occurs due to changes in the membrane permeability to Na^+ and K^+ ions. The membrane potential of an excitable cell (eg, nerve and muscle) cycles through the following stages:

1. **Resting potential (Choice A):** Usually equal to -70 mV. It is maintained by high resting membrane permeability to K^+ and low permeability to Na^+. K^+ efflux occurs via non-gated K^+ channels (leak channels). While at the resting potential, the inner side of the membrane is negatively charged with respect to the outer surface of the membrane.

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The graph depicts the potential voltage changes across a cell membrane; these changes (depolarization, repolarization, hyperpolarization, and resting potential) are collectively known as the action potential. The action potential occurs due to changes in the membrane permeability to Na^+ and K^+ ions. The membrane potential of an excitable cell (eg, nerve and muscle) cycles through the following stages:

1. **Resting potential (Choice A):** Usually equal to -70 mV. It is maintained by high resting membrane permeability to K^+ and low permeability to Na^+. K^+ efflux occurs via non-gated K^+ channels (leak channels). While at the resting potential, the inner side of the membrane is negatively charged with respect to the outer surface of the membrane.
2. **Depolarization:** Occurs due to opening of voltage-gated Na^+ channels with rapid influx of Na^+ into the cell. The large influx of Na^+ leads to an increased positive charge inside the membrane known as depolarization **(Choice B)**. Overshoot refers to the maximal value of the action potential during which the membrane potential obtains a positive value (approximately +35 mV) **(Choice C)**.
3. **Repolarization (Choice D):** Results from closure of Na^+ channels and simultaneous opening of K^+ channels. This causes a sharp decrease in the membrane permeability to Na^+ and a significant increase in K^+ permeance that exceeds that of the resting membrane. K^+ efflux is responsible for returning the membrane potential back to the resting potential.
4. **Hyperpolarization (Choice E):** Occurs because the voltage-gated K^+ channels remain open for a short time after repolarization is completed. The membrane potential thus becomes more negative than the normal resting potential and approaches the K^+ equilibrium potential of -85 mV. When the voltage-gated K^+ channels close, the membrane potential returns to the resting value maintained by the non-gated K^+ channels.

Educational objective:

The action potential results from changes in the membrane permeability to K^+ and Na^+ ions. Depolarization results from massive influx of Na^+ through voltage-gated Na^+ channels. Repolarization occurs due to closure of voltage-gated Na^+ channels and opening of voltage-gated K^+ channels. K^+ ion permeance is highest during the repolarization phase of the action potential.

Physiology	Nervous System	Resting membrane potential and action potential
Subject	System	Topic

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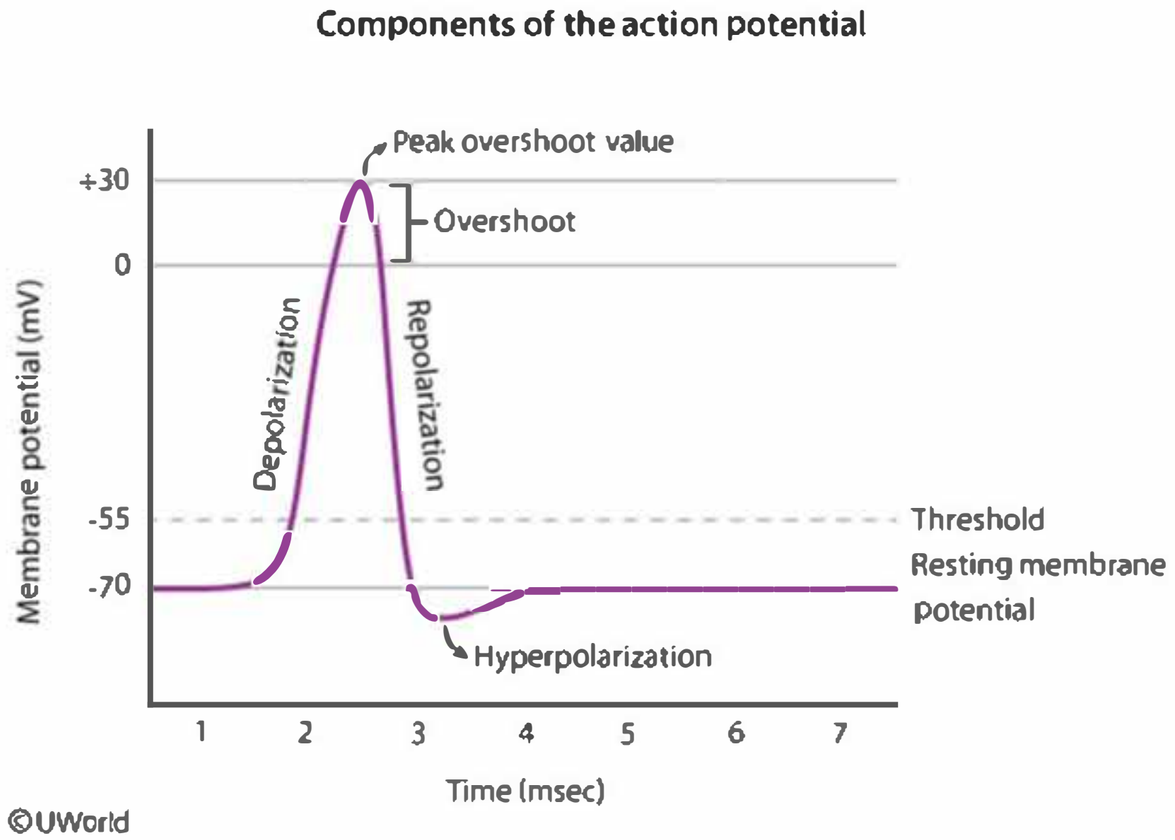
Exhibit Display



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A 4-year-old boy is brought to the hospital after several episodes of vomiting. The boy's mother reports that he was playing at a local park prior to the onset of illness. While cleaning him after the first episode of emesis, she found several small brown mushrooms clenched in his hands and brought samples with her. The boy is otherwise healthy and takes no medications. He is intubated due to somnolence and admitted to the intensive care unit. Analysis of the mushroom samples determines that the main poison stimulates muscarinic receptors. Which of the following is the most direct effect of this poison?

A. Detrusor muscle relaxation

B. Increased myocardial contractility

C. Kidney renin release

D. Nitric oxide synthesis

E. Pupillary dilation

F. Reduced salivation

Submit

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- A. Detrusor muscle relaxation (25%)
- B. Increased myocardial contractility (5%)
- C. Kidney renin release (3%)
- ✓ D. Nitric oxide synthesis (42%)
- E. Pupillary dilation (15%)
- F. Reduced salivation (7%)

Omitted
Correct answer
D

42%
Answered correctly

03 secs
Time Spent

04/14/2020
Last Updated

Explanation

Receptor	Target organ(s)	Effect of stimulation	Effect of inhibition

Receptor	Target organ(s)	Effect of stimulation	Effect of inhibition
M_1	Brain	Memory formation/cognitive functioning	Confusion
M_2	Heart	Decreased heart rate & atrial contraction	Increased heart rate & contractility
M_3	Peripheral vasculature	Smooth muscle relaxation, vasodilation, hypotension	Smooth muscle contraction, vasoconstriction, hypertension
	Lung	Bronchoconstriction	Bronchodilation
	Bladder	Detrusor contraction	Detrusor relaxation, urinary retention
	Eyes	Pupillary sphincter muscle contraction (miosis), ciliary muscle contraction (accommodation)	Mydriasis, cycloplegia, may precipitate acute angle glaucoma in elderly patients
	Gastrointestinal	Increased peristalsis, increased salivary & gastric secretions	Constipation, dry mouth, decreased acid production

M_3	Eyes	Pupillary sphincter muscle contraction (miosis), ciliary muscle contraction (accommodation)	Mydriasis, cycloplegia, may precipitate acute angle glaucoma in elderly patients
	Gastrointestinal	Increased peristalsis, increased salivary & gastric secretions	Constipation, dry mouth, decreased acid production
	Skin	Increased sweat production	Increased temperature (from decreased sweating)

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Muscarine, a toxin found in certain mushrooms, acts as a **muscarinic (M) agonist** in place of acetylcholine, resulting in an **increase in parasympathetic nervous system activity**. The M_2 and M_3 subtype receptors are responsible for most of the toxicities seen in patients.

Although the walls of peripheral blood vessels lack cholinergic innervation, M_3 receptors are present on the **endothelial** surface. Activation of M_3 receptors promotes **synthesis of nitric oxide** (NO), an endothelium-derived relaxing factor. NO diffuses into vascular smooth muscle cells, activating guanylate cyclase and increasing intracellular cyclic-GMP. Increased levels of cyclic-GMP activate **myosin light chain phosphatase**, which dephosphorylates myosin and prevents interaction of the myosin head with actin, resulting in **smooth muscle relaxation** and **vasodilation**. Vasodilation results in **hypotension**, with persistently low blood pressure leading to somnolence due to inadequate cerebral perfusion.

In contrast, activation of M_3 receptors in other sites leads to a G-protein-coupled increase in intracellular calcium, resulting in smooth muscle contraction. Clinically, this contraction manifests as detrusor bladder muscle contraction **(Choice A)**, pupillary constriction or miosis **(Choice E)**, and exocrine gland secretion (eg, salivation) **(Choice F)**.

(Choice B) M_2 receptors are predominantly found in cardiac muscle. Activation of M_2 receptors leads to a G-protein-coupled decrease in

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(Choice B) M_2 receptors are predominantly found in cardiac muscle. Activation of M_2 receptors leads to a G-protein-coupled decrease in intracellular cyclic-AMP and opens potassium channels to slow depolarization. This combination results in decreased inotropy (less contractility) and chronotropy (decreased heart rate).

(Choice C) Juxtaglomerular cells in the kidney release renin in response to decreased renal perfusion pressure. A muscarinic agonist would not have a direct effect on renin release, although the peripheral vasodilation and bradycardia might indirectly lead to renin release.

Educational objective:
Activation of muscarinic receptors by acetylcholine or cholinergic agonists results in peripheral vasodilation due to synthesis of nitric oxide in endothelial cells, which leads to vascular smooth muscle relaxation (eg, hypotension). Muscarinic receptor activation in other sites causes smooth muscle contraction.

References

- Muscarinic toxicity among family members after consumption of mushrooms.
- New pharmacological approaches to the cholinergic system: an overview on muscarinic receptor ligands and cholinesterase inhibitors.

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References

- Muscarinic toxicity among family members after consumption of mushrooms.
- New pharmacological approaches to the cholinergic system: an overview on muscarinic receptor ligands and cholinesterase inhibitors.

Physiology	Nervous System	Mushroom poisoning
Subject	System	Topic

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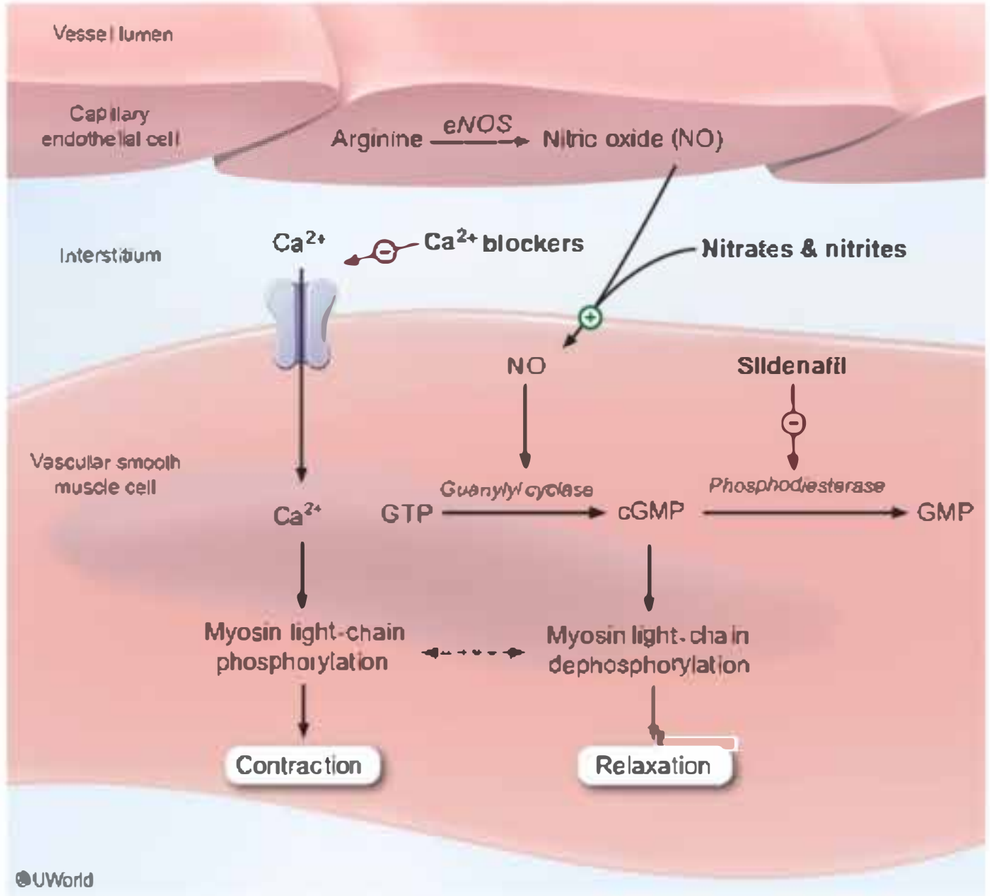
Pupillary sphincter

Exhibit Display

Mechanism of action of vasodilators



cGMP = cyclic guanosine monophosphate, eNOS = endothelial nitric oxide synthase, GMP = guanosine monophosphate, GTP = guanosine 5'-triphosphate

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intracellular cyclic-AMP and opens potassium channels to slow depolarization. This combination results in decreased inotropy (less contractility)

A 23-year-old woman is referred to a neurologist due to recent-onset diplopia and ataxia. She has not had similar symptoms before. However, about a year ago, she experienced numbness and paresthesia involving her left leg that have since resolved. After a comprehensive neurological examination, the physician orders an MRI of the brain, which reveals several areas of T2 hyperintensity consistent with axonal demyelination. A diagnosis of multiple sclerosis is made. Which of the following neuronal properties is most likely to decrease as a direct result of demyelination?

A. Length (space) constant

B. Spatial summation

C. Temporal summation

D. Threshold

E. Time constant

Submit

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- ✓ A. Length (space) constant (45%)
- B. Spatial summation (9%)
- C. Temporal summation (16%)
- D. Threshold (2%)
- E. Time constant (24%)

Omitted
Correct answer
A

45%
Answered correctly

02 secs
Time Spent

05/15/2020
Last Updated

Explanation

Multiple sclerosis is an immune-mediated demyelinating disease of the central nervous system. Myelin is an electrical insulator and increases the conduction velocity of action potentials; demyelination leads to slowing of the impulses with resultant neurological deficits.

The speed of conduction down an axon depends on 2 constants: the length constant and the time constant (ie, **velocity = length/time**).

- The length constant, also known as the space constant, is a measure of how far along an axon an electrical impulse can propagate without requiring active regeneration by ion channels. It is based on the relative resistance of conduction along the axon (within the cytoplasm) [illegible]

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- The length constant, also known as the space constant, is a measure of how far along an axon an electrical impulse can propagate without requiring active regeneration by ion channels. It is based on the relative resistance of conduction along the axon (within the cytoplasm) compared to the resistance across the membrane. Myelin increases the length constant by reducing charge dissipation across the membrane (increasing membrane resistance). This allows the electrical impulse from individual sodium channels to travel farther, allowing activation of more distant channels. As such, demyelination will decrease the length constant and result in shorter impulse conduction.
- The time constant is a measure of the time it takes for the membrane potential to respond to a change in membrane permeability (ie, sodium channel activation) and is based on membrane resistance and capacitance. Myelin decreases membrane capacitance (reduces the amount of charge stored by the membrane) and increases membrane resistance (reduces charge leakage through the membrane) in axon segments between the nodes of Ranvier; this reduces the time constant and allows the membrane potential to change faster. Demyelination would increase the time constant and result in slower changes in membrane voltage.

Therefore, **demyelination** decreases neuronal signaling velocity both by **decreasing the length constant** and increasing the time constant (ie, ↓ velocity = ↓ length / ↑ time) **(Choice E)**.

(Choices B and C) Summation refers to the additive effects of multiple postsynaptic potentials on a target neuron's membrane potential. Summation can occur in the dendrites, cell body, and axon hillock but not in the axon. Temporal summation refers to the combined effect of sequential impulses from the same neuron over time, whereas spatial summation refers to the combined effect of simultaneous impulses from several different neurons.

(Choice D) Threshold refers to the membrane potential value required to initiate an action potential. It is determined by the intrinsic properties of the voltage-gated sodium channels present in the membrane.

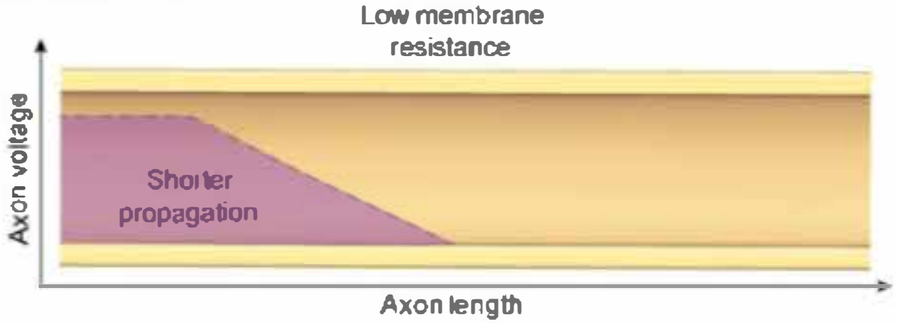
Educational objective:
The speed of conduction down an axon depends on 2 constants: the length constant and the time constant (ie, velocity = length/time). Myelination increases the length constant and decreases the time constant, both of which improve axonal conduction speed. Demyelination thus impairs

Exhibit Display

Length constant of the neuron

The distance an impulse can propagate depends on the membrane resistance compared to the axon (internal) resistance

Unmyelinated neuron



Myelinated neuron

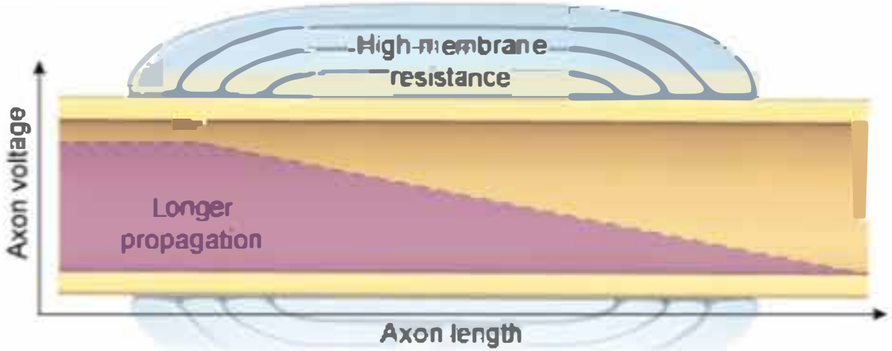


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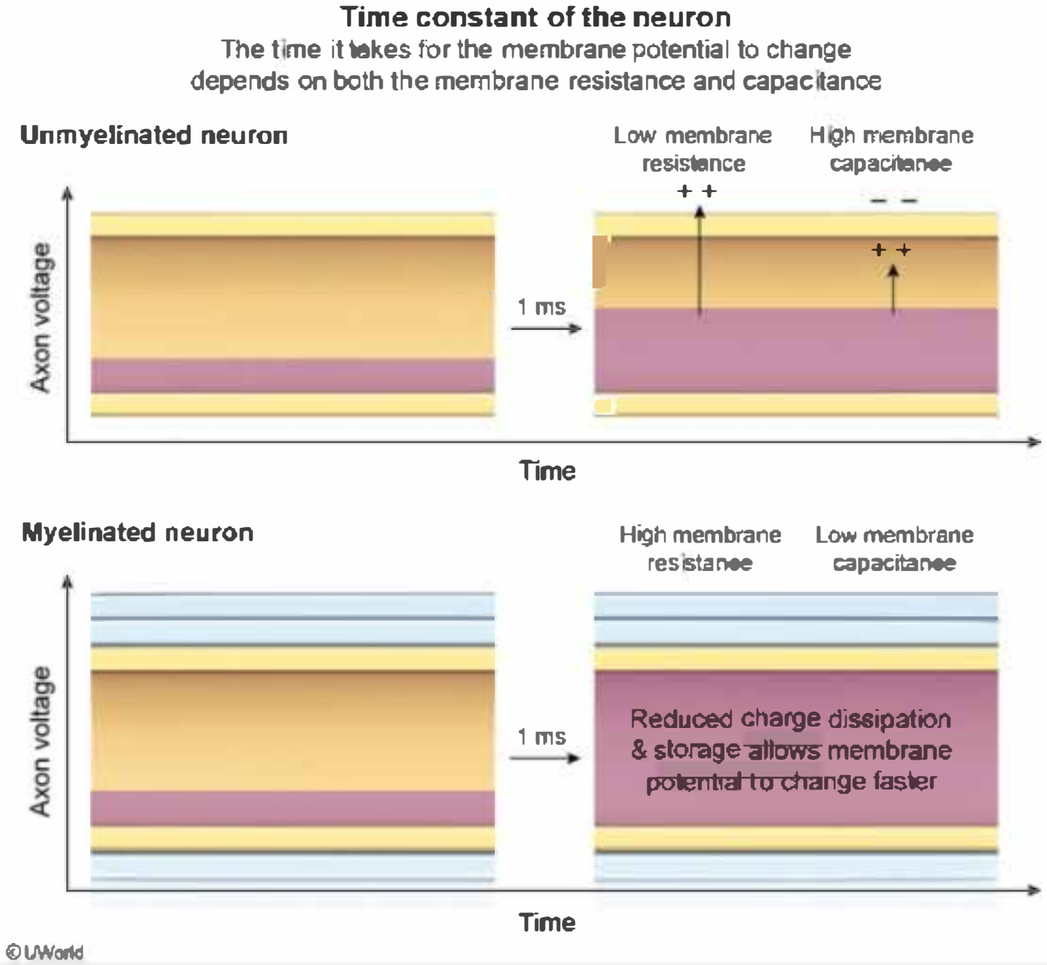
Exhibit Display



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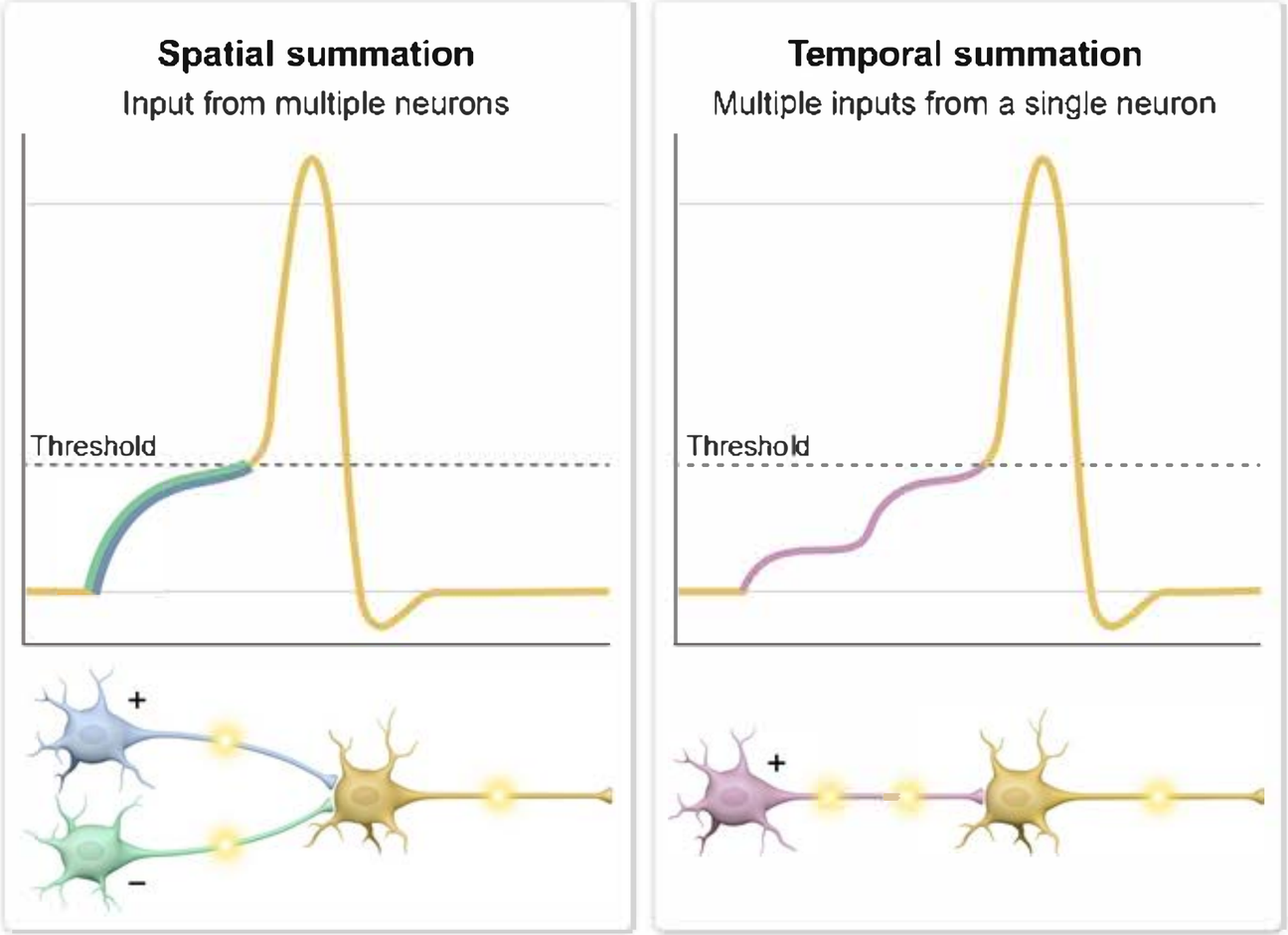

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Educational objective:
The speed of conduction down an axon depends on 2 constants: the length constant and the time constant (ie, velocity = length/time). Myelination increases the length constant and decreases the time constant, both of which improve axonal conduction speed. Demyelination thus impairs stimulus transmission.

References

- Multiple sclerosis: the disease and its manifestations.
- The pathophysiology of multiple sclerosis: the mechanisms underlying the production of symptoms and the natural history of the disease.

Physiology	Nervous System	Multiple sclerosis
Subject	System	Topic

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A researcher is investigating a new antiseizure drug that binds to and activates GABA-A receptors in the central nervous system. During the experiment, she isolates a nerve and uses a microelectrode to measure its membrane potential under physiologic conditions. The resting potential of the nerve is found to be −70 mV. Which of the following membrane potentials will most likely be recorded from this neuron following exposure to the new drug?

A. −75 mV
B. −70 mV
C. −55 mV
D. 0 mV
E. +25 mV
F. +40 mV
G. +60 mV
H. +125 mV

Submit

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- ✓ A. −75 mV (74%)
- B. −70 mV (8%)
- C. −55 mV (6%)
- D. 0 mV (2%)
- E. +25 mV (1%)
- F. +40 mV (1%)
- G. +60 mV (3%)
- H. +125 mV (1%)

Omitted
Correct answer
A

74%
Answered correctly

02 secs
Time Spent

04/29/2020
Last Updated

Explanation

Equilibration movements of charged ions under physiologic conditions

Equilibration movements of charged ions under physiologic conditions

Ion	Charge	Major location	Equilibrium potential	Equilibration movement at -70 mV
Sodium	Positive	Extracellular	+ 60 mV	Extracellular gradient drives Na^+ into cell, making membrane potential more positive
Potassium	Positive	Intracellular	- 90 mV	Intracellular gradient drives K^+ out of cell, making membrane potential more negative
Chloride	Negative	Extracellular	- 75 mV	Extracellular gradient drives Cl^- into cell, making membrane potential more negative
Calcium	Positive	Extracellular	+ 125 mV	Extracellular gradient drives Ca^{2+} into cell, making membrane potential more positive

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The **GABA-A receptor** is an ionotropic receptor (eg, part of an ion channel) that regulates the flow of negatively charged **chloride ions** across the neuronal cell membrane. A drug that binds to and activates GABA-A receptors will increase the conductance of chloride ions, causing passive transport down the concentration gradient into the cell interior. This causes the membrane potential to become **hyperpolarized** (more negative

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(Choice B) Exposure to the experimental drug will make the neuronal membrane potential more negative than the resting membrane potential due to the opening of chloride channels.

(Choice C) The opening of ligand-gated (controlled by binding of neurotransmitters) sodium channels allows for the initial influx of positively charged sodium ions. This causes a graded depolarization of the neuronal cell membrane toward the threshold for firing an action potential (−55 mV).

(Choices D, E, F, and G) Once the threshold membrane potential is reached, fast voltage-gated sodium channels open to mediate the upstroke phase of the neuronal action potential. During this time, the membrane potential becomes even more positive due to the rapid influx of sodium ions and causes the membrane potential to approach the equilibrium potential for sodium (+60 mV).

(Choice H) The influx of positively charged calcium ions can raise the membrane potential even further (more positive than +60 mV) toward the equilibrium potential for calcium ions (+125 mV).

Educational objective:
A drug that binds to and activates GABA-A receptors (or enhances their activity) will increase the conductance of chloride ions, leading to increased passive transport of chloride into the cell interior. This causes the membrane potential to become hyperpolarized (more negative than the resting membrane potential) by approaching or reaching the equilibrium potential for chloride.

References

- Generation of resting membrane potential.

Physiology	Nervous System	Resting membrane potential and action potential
Subject	System	Topic

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References

- Generation of resting membrane potential.

Physiology	Nervous System	Resting membrane potential and action potential
Subject	System	Topic

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A 18-year-old man is brought to the emergency department after sustaining a traumatic brain injury during a motor vehicle collision. On arrival, the patient is comatose and has a Glasgow Coma Scale score of 3. His blood pressure is 110/70 mm Hg, and pulse is 114/min. Pupils are miotic, equal, and reactive to light. Ecchymosis is present behind the ear, but the remainder of the trauma survey is unremarkable. Rapid-sequence intubation is performed, and the patient is mechanically ventilated. A noncontrast head CT scan demonstrates bifrontal contusions and a basilar skull fracture. One day later, a repeat head CT scan reveals diffuse cerebral edema. The ventilator respiratory rate is adjusted to achieve a $PaCO_2$ level of 26-30 mm Hg. Which of the following is the most likely effect of this intervention?

A. Decreased brain metabolic demand

B. Increased cerebral perfusion

C. Increased cerebral blood volume

D. Increased cerebral vascular resistance

E. Increased displacement of cerebrospinal fluid into the thecal sac

Submit

A 19-year-old man is brought to the emergency department after sustaining a traumatic brain injury during a motor vehicle collision. On arrival, the patient is comatose and has a Glasgow Coma Scale score of 3. His blood pressure is 110/70 mm Hg, and pulse is 114/min. Pupils are miotic, equal, and reactive to light. Ecchymosis is present behind the ear, but the remainder of the trauma survey is unremarkable. Rapid-sequence intubation is performed, and the patient is mechanically ventilated. A noncontrast head CT scan demonstrates bifrontal contusions and a basilar skull fracture. One day later, a repeat head CT scan reveals diffuse cerebral edema. The ventilator respiratory rate is adjusted to achieve a $PaCO_2$ level of 26-30 mm Hg. Which of the following is the most likely effect of this intervention?

A. Decreased brain metabolic demand (12%)

B. Increased cerebral perfusion (19%)

C. Increased cerebral blood volume (1%)

✓ D. Increased cerebral vascular resistance (61%)

E. Increased displacement of cerebrospinal fluid into the thecal sac (5%)

Omitted
Correct answer
D

61%
Answered correctly

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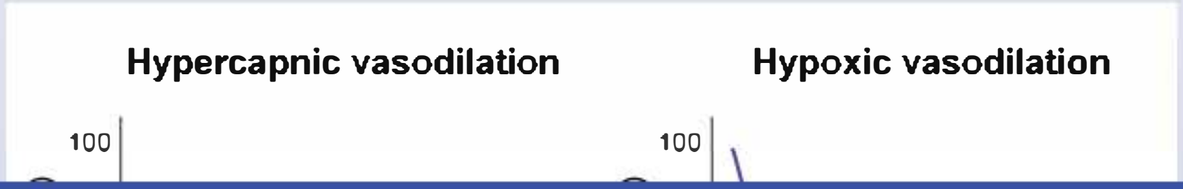
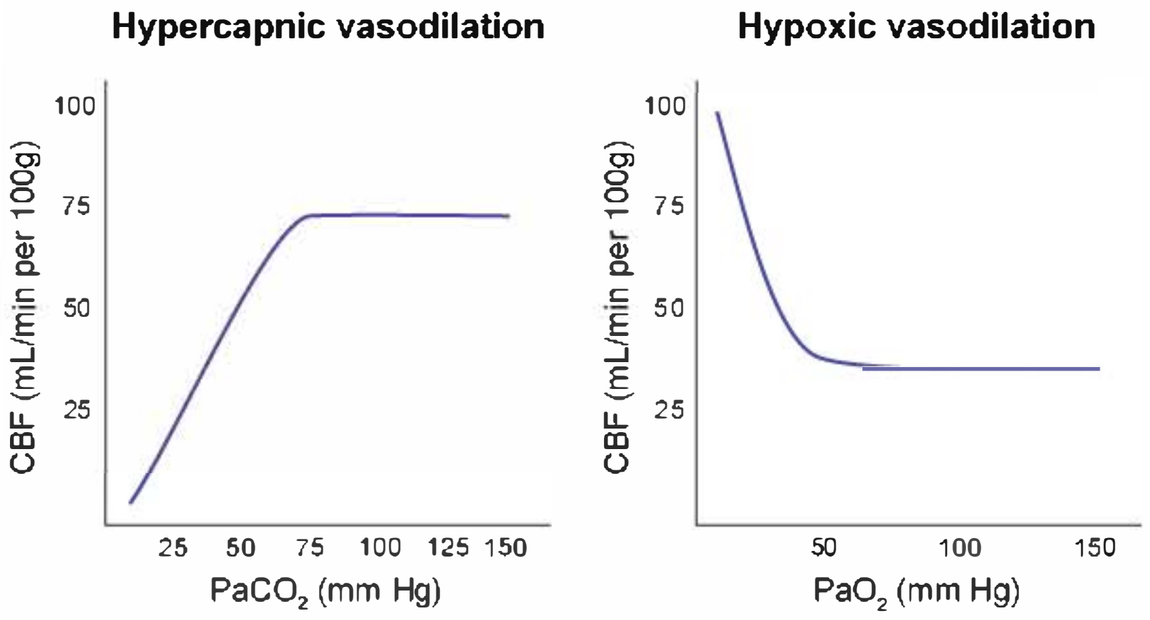
Time Spent

04/21/2020
Last Updated

Explanation





CBF = cerebral blood flow.

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The brain has little room for expansion as it is encased in the cranium. A small volume change in any of the intracranial components (eg, brain tissue, blood, cerebrospinal fluid [CSF]) can produce significant changes in intracranial pressure (ICP). Therefore, even small increases in cerebral blood volume can raise ICP and cause brain compression.

The main factors influencing cerebral circulation are systemic blood pressure and arterial blood gas levels. When systemic blood pressure is 60-140 mm Hg, it has little effect on cerebral blood volume because autoregulation (via cerebral blood vessel dilation and contraction) keeps blood flow constant. Blood pressure >150 mm Hg increases cerebral vascular volume and blood flow, causing a corresponding increase in ICP. In contrast, blood pressure <50 mm Hg causes cerebral hypoperfusion and potential ischemia.

Arterial blood gases also have a powerful effect on cerebral blood flow, with $PaCO_2$ being the most important regulator. A **drop in $PaCO_2$** due to hyperventilation causes **vasoconstriction**. The resulting reduction in cerebral blood volume **(Choice C)** leads to decreased ICP. Lowering

The brain has little room for expansion as it is encased in the cranium. A small volume change in any of the intracranial components (eg, brain tissue, blood, cerebrospinal fluid [CSF]) can produce significant changes in intracranial pressure (ICP). Therefore, even small increases in cerebral blood volume can raise ICP and cause brain compression.

The main factors influencing cerebral circulation are systemic blood pressure and arterial blood gas levels. When systemic blood pressure is 60-140 mm Hg, it has little effect on cerebral blood volume because autoregulation (via cerebral blood vessel dilation and contraction) keeps blood flow constant. Blood pressure >150 mm Hg increases cerebral vascular volume and blood flow, causing a corresponding increase in ICP. In contrast, blood pressure <50 mm Hg causes cerebral hypoperfusion and potential ischemia.

Arterial blood gases also have a powerful effect on cerebral blood flow, with $PaCO_2$ being the most important regulator. A **drop in $PaCO_2$** due to hyperventilation causes **vasoconstriction**. The resulting reduction in cerebral blood volume **(Choice C)** leads to decreased ICP. Lowering $PaCO_2$ is one of the measures employed to **reduce ICP** in mechanically ventilated patients with cerebral edema.

(Choice A) The brain has a very large oxygen requirement, about 20% of all O_2 consumed by the body. Induced sedation and therapeutic hypothermia can decrease brain metabolic demand, exerting a neuroprotective effect and improving ICP by reducing cerebral blood volume.

(Choice B) The vasoconstriction induced by hyperventilation can cause a decrease in local cerebral perfusion that can worsen neurologic injury in patients with acute traumatic brain injury or stroke. Therefore, hyperventilation should be used with caution in these patients, and the $PaCO_2$ should be maintained $\geq$30 mm Hg.

(Choice E) The thecal sac is a sheath of dura mater that contains CSF and surrounds the spinal cord. Increased ICP can cause displacement of CSF from the brain into the thecal sac. However, the drop in ICP caused by hyperventilation reduces CSF displacement.

Educational objective:
Carbon dioxide is a potent vasodilator of cerebral vasculature. Tachypnea causes hypocapnia and cerebral vasoconstriction, thereby decreasing cerebral blood volume and intracranial pressure.

Physiology	Nervous System	Traumatic brain injury
Subject	System	Topic

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